Complete Summary

GUIDELINE TITLE

National Academy of Clinical Biochemistry and IFCC Committee for standardization of markers of cardiac damage laboratory medicine practice guidelines: Analytical issues for biochemical markers of acute coronary syndromes.

BIBLIOGRAPHIC SOURCE(S)

Apple FS, Jesse RL, Newby LK, Wu AH, Christenson RH, Cannon CP, Francis G, Morrow DA, Ravkilde J, Storrow AB, Tang W, IFCC Committee on Standardization of Markers of Cardiac Damage, Jaffe AS, Mair J, Ordonez-Llanos J, Pagani F, Panteghini M, Tate J, National Academy of Clinical Biochemistry. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: analytical issues for biochemical markers of acute coronary syndromes. Clin Chem 2007 Apr;53(4):547-51. [23 references] PubMed

Apple FS, Jesse RL, Newby LK, Wu AH, Christenson RH, National Academy of Clinical Biochemistry, IFCC Committee for Standardization of Markers of Cardiac Damage. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: Analytical issues for biochemical markers of acute coronary syndromes. Circulation 2007 Apr 3;115(13):e352-5. [23 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- June 8, 2007, Troponin-I Immunoassay: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Acute coronary syndrome (ACS)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Internal Medicine
Pathology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS)
- To address analytical issues for cardiac biomarkers

TARGET POPULATION

Patients with suspected or known acute coronary syndrome (ACS)

INTERVENTIONS AND PRACTICES CONSIDERED

Use of cardiac biomarkers

- Reference decision-limits for cardiac biomarkers
- Acceptable specimens for cardiac biomarker analyses

MAJOR OUTCOMES CONSIDERED

Usefulness and effectiveness of pre-analytical and analytical biomarker assay characteristics for acute coronary syndrome (ACS)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

These National Academy of Clinical Biochemistry (NACB) guidelines were developed rigorously; however it was possible to include only papers published in the English language. The specified method for developing the evidence base for recommendations listed involved use of PubMed, EMBASE, and other databases that were not necessarily published. Systematic methods were used whenever available; searches were first set to be sensitive to avoid missing papers of possible interest, and then narrowed to sort through the literature in order to enhance specificity. The writing group contacted recognized experts to assure that important evidence had not been missed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

B - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries

C - Expert Consensus was the primary basis for the recommendation

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Academy of Clinical Biochemistry's (NACB) Laboratory Medicine Practice Guidelines (LMPG) for use of cardiac markers in coronary artery diseases were published in July of 1999. Since production of this initial document, numerous published studies and presented data have added significantly to the knowledge base for cardiac biomarkers. This increased knowledge has substantially expanded the scope of recommendations for cardiac biomarker utilization since the 1999 document, and in particular has required the inclusion of recommendations regarding biomarkers that extend beyond myocardial necrosis. Toward addressing these advances and their impact on biomarker utilization in clinical practice, the NACB appointed a chair and members of a LMPG committee that was charged with the overall objective of revising and extending the earlier recommendations by establishing modern guidelines for Utilization of Biomarkers in Acute Coronary Syndrome and Heart Failure. This LMPG is aimed at providing analytical and clinical guidance for the measurement and interpretation of cardiac biochemical markers of acute coronary syndromes (ACS), heart failure and point-of-care measurement and logistics of providing ACS biomarker data for patient care; guidance for interpretation of biomarkers in etiologies other than ACS and Heart Failure is included as well.

These guidelines and their recommendations are structured into six chapters that include Chapter 1: Clinical Utilization of Biomarkers in Acute Coronary Syndromes (ACS); Chapter 2: Analytical Issues of ACS Biomarkers; Chapter 3: Clinical Utilization of Biomarkers of Heart Failure; Chapter 4: Analytical Issues of Heart Failure Biomarkers; Chapter 5: Point of Care Testing and Logistics; and Chapter 6: Cardiac Biomarkers and Other Etiologies. Each chapter was spearheaded by a

writing group, which was a subset of the overall committee. In addition, other ad hoc expertise contributed to the writing group of some subsections and chapters to optimize the content and quality of the guidelines. The "questions" for each chapter are in the form of issues addressed and specified in the organization of each individual chapter. The chapter design of the guidelines was used to facilitate finding guidance by users; this format was also used, in part, to provide an easy and focused procedure for updating the guidelines in the future. Also, the chapter design allowed publication of sections in appropriate laboratory medicine and clinical specialty journals.

Stakeholder involvement in development and refinement of these guidelines was substantial. The guideline team was comprised of laboratory medicine, ACS cardiology experts, and heart failure cardiology experts. As these guidelines target acutely ill patients, Emergency Medicine stakeholders were represented by a specialist; it is also noteworthy that all of the laboratory professionals and cardiology experts on the guideline committee have substantial interaction, knowledge, and publications in the area of laboratory and clinical medicine in the Emergency Medicine environment.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Modified American College of Cardiology/American Heart Association Classifications: Summary of Indications

Class I: Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or treatment.

> **Class IIa**: Weight of evidence/opinion is in favor of usefulness/efficacy.
>
> **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Stakeholder involvement in development and refinement of these guidelines was substantial. To further enhance stakeholder input, draft revisions of the Guidelines were prepared and placed for comment on the National Academy of Clinical Biochemistry (NACB) World Wide Web site (http://www.aacc.org/AACC/members/nacb/LMPG/OnlineGuide/DraftGuidelines/BioHearFailure/). The draft Laboratory Medicine Practice Guidelines (LMPG) and suggested revisions were also presented for public and stakeholder comment at the October 2004 Arnold O. Beckman Conference titled *Cardiac Markers: Establishing Guidelines and Improving Results*. Refer to Table 1 of the Preamble to the original guideline document for a list of the various stakeholder groups that agreed to examine the documents and were represented at the conference.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the weight of evidence (A-C) and the summary of indications (Classes I, II, IIa, IIb, III) are presented at the end of the "Major Recommendations" field.

Note from the National Academy of Clinical Biochemistry (NACB) and the National Guideline Clearinghouse (NGC)*: The Laboratory Medicine Practice Guidelines (LMPG) for utilization of biochemical markers in acute coronary syndromes and heart failure* have been divided into individual summaries. In addition to the current summary, the following are available:

- Chapter 1: Clinical characteristics and utilization of biochemical markers in acute coronary syndromes
- Chapter 3: Clinical utilization of cardiac biomarker testing in heart failure
- Chapter 4: Analytical issues for biomarkers of heart failure
- Chapter 5: Point of care testing, oversight and administration of cardiac biomarkers for acute coronary syndromes
- Chapter 6: Use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure

Analytic Biomarker Issues

Recommendations: Analytical Aspects of Acute Coronary Syndrome (ACS) Biomarkers

All Class I

1. Reference decision-limits should be established for each cardiac biomarker based on a population of normal, healthy individuals without a known history of heart disease (reference population). For cardiac troponin I (cTnI) and T (cTnT), as well as for creatine kinase MB (CK-MB) mass, the 99th percentile of the reference population should be the decision-limit for myocardial injury. The Clinical Laboratory Standards Institute (CLSI; formerly NCCLS) recommends a minimum of 120 individuals per group of healthy individuals for appropriate statistical determination of a normal reference limit cutoff.

Sex-specific reference limits should be used in clinical practice for CK-MB mass. For myoglobin, the 97.5th percentile (with sex-specific reference limits) should be the decision-limit for myocardial injury. **(Level of Evidence: B)**

2. One decision-limit, the 99th percentile, is recommended as the optimum cutoff for cTnI, cTnT, and CK-MB mass. ACS patients with cTnI and cTnT results above the decision-limit should be labeled as having myocardial injury and a high-risk profile. **(Level of Evidence: B)**
3. Assays for cardiac biomarkers should strive for a total imprecision (% coefficient of variation [CV]) of <10% at the 99th percentile reference limit. Before introduction into clinical practice, cardiac biomarker assays must be characterized with respect to potential interferences, including rheumatoid factors, human anti-mouse antibodies, and heterophile antibodies. Pre-analytical and analytical assay characteristics should include biomarker stability (over time and across temperature ranges) for each acceptable specimen type used in clinical practice and identification of antibody/epitope recognition sites for each biomarker. Analytical and pre-analytical specifications developed by professional groups such as the International Federation of Clinical Chemistry (IFCC) should be followed. **(Level of Evidence: C)**
4. Serum, plasma, and anticoagulated whole blood are acceptable specimens for the analysis of cardiac biomarkers. Choice of specimen must be based on sufficient evidence and the known characteristics of individual biomarker assays. **(Level of Evidence: C)**

Definitions:

Weight of Evidence

A - Data derived from multiple randomized or appropriately designed clinical trials that involved large numbers of patients

B - Data derived from a limited number of randomized or appropriately designed trials that involved small numbers of patients or from careful analyses of observational registries.

C - Expert Consensus was the primary basis for the recommendation

Summary of Indications

Class I: Conditions for which there is evidence and/or general agreement that a given laboratory procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a laboratory procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the laboratory procedure/treatment is not useful/effective and in some cases may be harmful.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate utilization of biochemical markers in the evaluation, risk stratification, and management of acute coronary syndromes (ACS)

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The materials in this publication represent the opinions of the authors and committee members, and do not necessarily represent the official position of the National Academy of Clinical Biochemistry (NACB) or the International Federation of Clinical Chemistry (IFCC). The National Academy of Clinical Biochemistry is the academy of the American Association for Clinical Chemistry.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Apple FS, Jesse RL, Newby LK, Wu AH, Christenson RH, Cannon CP, Francis G, Morrow DA, Ravkilde J, Storrow AB, Tang W, IFCC Committee on Standardization of Markers of Cardiac Damage, Jaffe AS, Mair J, Ordonez-Llanos J, Pagani F, Panteghini M, Tate J, National Academy of Clinical Biochemistry. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: analytical issues for biochemical markers of acute coronary syndromes. Clin Chem 2007 Apr;53(4):547-51. [23 references] PubMed

Apple FS, Jesse RL, Newby LK, Wu AH, Christenson RH, National Academy of Clinical Biochemistry, IFCC Committee for Standardization of Markers of Cardiac Damage. National Academy of Clinical Biochemistry and IFCC Committee for Standardization of Markers of Cardiac Damage Laboratory Medicine Practice Guidelines: Analytical issues for biochemical markers of acute coronary syndromes. Circulation 2007 Apr 3;115(13):e352-5. [23 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Jul (revised 2007 Apr)

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

GUIDELINE COMMITTEE

The National Academy of Clinical Biochemistry

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

National Academy of Clinical Biochemistry (NACB) Writing Group Members: Fred S. Apple, Robert L. Jesse, L. Kristin Newby, Alan H.B. Wu, Robert H. Christenson

NACB Committee Members: Robert H. Christenson, *Chair*, University of Maryland School of Medicine, Baltimore, Maryland, USA; Fred S. Apple, Hennepin County Medical Center and University of Minnesota, Minneapolis, Minnesota, USA; Christopher P. Cannon, Brigham and Women's Hospital, Boston, Massachusetts, USA; Gary S. Francis, Cleveland Clinic Foundation, Cleveland, Ohio, USA; Robert L. Jesse, Medical College of Virginia, Richmond, Virginia, USA; David A. Morrow, Brigham and Women's Hospital, Boston, Massachusetts, USA; L. Kristin Newby, Duke University Medical Center, Durham, North Carolina, USA; Jan Ravkilde, Aarhus University Hospital, Aarhus, Denmark; Alan B. Storrow, Vanderbilt University, Nashville, Tennessee, USA; W. H. Wilson Tang, Cleveland Clinic Foundation, Cleveland, Ohio, USA; Alan H. B. Wu, San Francisco General Hospital and University of California at San Francisco, San Francisco, California, USA

Ad Hoc members of the committee for selected sections: Allan S. Jaffe, Mayo Clinic, Rochester, Minnesota, USA; Alan S. Maisel, University of California at San Diego, San Diego, California, USA; Mauro Panteghini, University of Milan, Milan, Italy

IFCC Committee On Standardization Of Markers Of Cardiac Damage (C-SMCD) members: Fred S. Apple, *Chair*; Robert H. Christenson; Allan S. Jaffe, Rochester, MN; Johannes Mair, Innsbruck, Austria; Jordi Ordonez-Llanos, Barcelona, Spain; Franca Pagani, Brecia, Italy; Mauro Panteghini, Milan, Italy; Jillian Tate, Brisbane, Australia; Alan H.B. Wu

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Financial Disclosures: The National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines Committee for Utilization of Biomarkers in Acute Coronary Syndromes and Heart Failure reports all reported relationships within the 2 years previous to this publication that may be relevant to this guidelines document. A document of those relationships may be found in the online Data Supplement at http://www.clinchem.org/content/vol53/issue4.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Preamble. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for utilization of biochemical markers in acute coronary syndromes and heart failure. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2007. p. 1-3.

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site.

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 11, 2008. The information was verified by the guideline developer on April 2, 2008.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and

related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/15/2008